PB82-247214

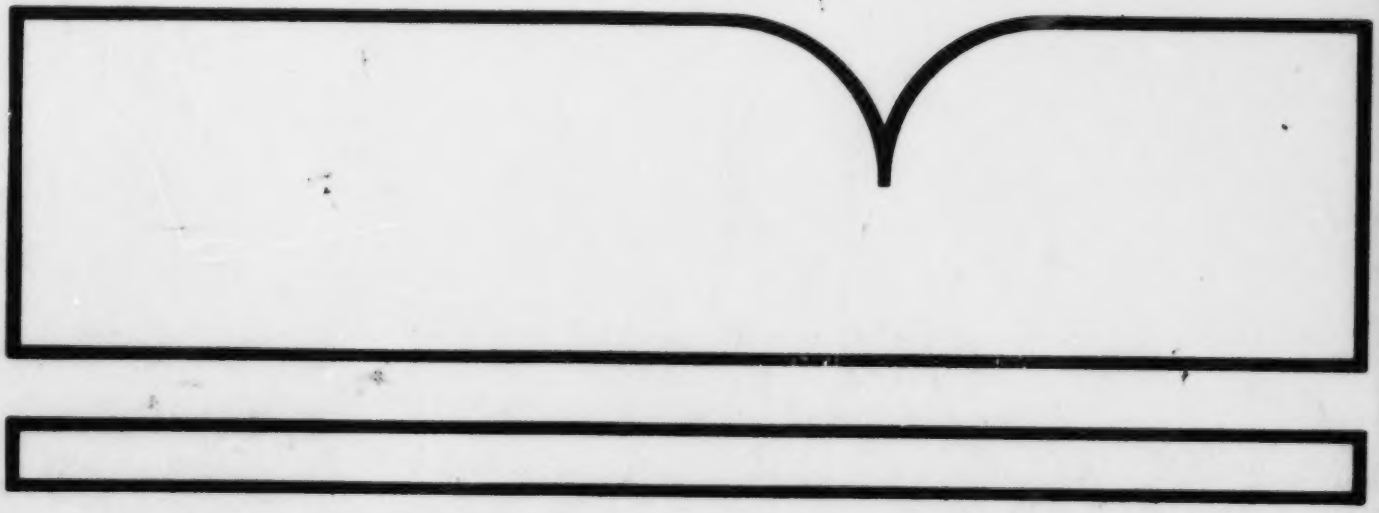
Effects of Age and Body Lead Burden on CNS Function in Young Children. II. EEG Spectra

North Carolina Univ. at Chapel Hill

Prepared for

Health Effects Research Lab.
Research Triangle Park, NC

12 May 81



U.S. Department of Commerce
National Technical Information Service
NTIS

TECHNICAL REPORT DATA (Please read Instructions on the reverse before completing)		
1. REPORT NO. EPA-600/J-80-173	2. JOURNAL ARTICLE	3. RECIPIENT'S ACCESSION NO. PB82-241214
4. TITLE AND SUBTITLE Effects of Age and Body Lead Burden on CNS Function in Young Children II - EEG Spectra		5. REPORT DATE
		6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S) V.A. Benignus*, D.A. Otto*, K.E. Muller, and K.J. Seiple (*EPA)		8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS Departments of Phychology, Biostatistics, & Epidemiology University of North Carolina Chapel Hill, NC 27514		10. PROGRAM ELEMENT NO.
		11. CONTRACT/GRANT NO. Contract No: 68-02-1702
12. SPONSORING AGENCY NAME AND ADDRESS Office of Research and Development Health Effects Research Laboratory US Environmental Protection Agency Research Triangle Park, NC 27711		13. TYPE OF REPORT AND PERIOD COVERED
		14. SPONSORING AGENCY CODE EPA-600/11

15. SUPPLEMENTARY NOTES

Published In: Electroencephalography and Clinical Neurophysiology 52: 240-248, 1981

16. ABSTRACT

This study explored the effects of age and PbB upon EEG power spectra and various measures of hemispheric laterality in children, aged 13-75 months, watching a display(cartoon). The following are the principle conclusions:

1-The δ- and θ-band amplitude decreased aith age

2-When only bilaterally synchronized EEG between P3 and P4 was considered, the amplitude of P3 was estimated as greater than P4 in all frequency bands and for all ages. Previous reports have not shown lateral EEG dominance in children below 75 months.

3-When lateral dominance measures consider only the relationship between synchronized EEG at P3 and P4, bilateral communality in the δ band increased with age.

4-Increased PbB generally produced an increase in the relative amplitude of synchronized EEG between P3 and P4 in all frequency bands. This was true for PbB levels well below 15 µg/dl, among the lowest level PbB effects previously reported. No clinical or behavioral effects of PbB values have been reported below 15 µg/dl.

Greater understanding of these data would help define the extent of PbB effects on the CNS

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS (This Report)	21. NO. OF PAGES
Release to Public	Unclassified	
	20. SECURITY CLASS (This page) Unclassified	22. PRICE

PB82-247214 EPA-600/J-80-173
JOURNAL ARTICLE

Electroencephalography and Clinical Neurophysiology, 1981, 52: 240—248
Elsevier/North-Holland Scientific Publishers, Ltd.

EFFECTS OF AGE AND BODY LEAD BURDEN ON CNS FUNCTION IN YOUNG CHILDREN. II. EEG SPECTRA

V.A. BENIGNUS [1], D.A. OTTO [1], K.E. MULLER [2] and K.J. SEIPLE [3]

U.S. Environmental Protection Agency, MD-58, Research Triangle Park, N.C. 27711 (U.S.A.)

(Accepted for publication: May 12, 1981)

Low level lead (Pb) exposure has been shown to have behavioral effects in children (Otto et al. 1981), but there have been only unquantified case reports of EEG effects. Burrows et al. (1951), Bradley and Powell (1954), Byers and Maloof (1954), Thurston et al. (1955), Smith et al. (1963) and Fejerman et al. (1973) reported such symptoms as slowed alpha frequency, reduced EEG amplitudes, dysrhythmic activity and sometimes seizure-like activity. These reports involved high levels of Pb exposure which were associated with overt clinical symptoms. In one case where Pb values below 60 μg/dl were reported, EEGs were normal by visual classification (Smith et al. 1963).

EEG spectra in children were shown to be a function of age by Matousek and Petersen (1973). From 1 through 15 years, low frequency EEG amplitude diminished. Amplitude in alpha (α) spectral bands increased slightly over age. The peak frequency of rhythmic α waves increased as a function of age, first appearing at about 3 months in the 3.5 Hz range and approaching the 10 Hz range at 7—10 years.

Development of lateral dominance in EEG of children is less well documented due partly to methodological differences among investigators (Donchin et al. 1977). No consistent lateral dominance has been demonstrated in the EEG of children below the age of 11 years even though handedness appears at about 3 years (Giannitrapani et al. 1966; Joseph et al. 1976; Varner et al. 1977). Measures of cerebral dominance used in these studies were ratios or differences of amplitudes and phase relationships. These measures were computed using either total EEG amplitude, selected frequency bands or specific rhythmic activity such as the α wave.

Typically measures of laterality describe the relationship between *total* activity at each pair of sites, both synchronized and unsynchronized. Possibly the critical relationships are those between bilaterally synchronized waves only. It is possible, conceptually and analytically, to separate left and right hemisphere EEG into bilaterally synchronized waves and bilaterally unsynchronized waves (random with respect to each other). Least squares estimators have been defined for two sites of measurement which describe the relationship of the synchronized activity *only* and exclude all non-synchronized activity (Bendat and Piersol 1971). These measures include the 'coherence spectrum' which is one multiple correlation between synchronized portions of two EEG waves in each frequency band. The 'gain spectrum' is one regression coefficient for the relationship between the synchronized portions of two

[1] U.S. Environmental Protection Agency and Department of Psychology, University of North Carolina, Chapel Hill, N.C. 27514, U.S.A.
[2] Department of Biostatistics, University of North Carolina, Chapel Hill, N.C. 27514, U.S.A.
[3] Department of Epidemiology, University of North Carolina, Chapel Hill, N.C. 27514, U.S.A.

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA 22161

EEG waves in each frequency band. 'Phase' estimates the time delay between two synchronized waves in each frequency band.

Gain is interpretable as the amplification of a signal path between left and right hemisphere (Gersch and Tharp 1976) and coherence as a measure of signal-to-noise ratio (Bendat and Piersol 1971). Galbraith (1967), Busk and Galbraith (1975) and Livanov (1977) argued that when coherence is high between two CNS sites, then information is being transmitted between those sites. Busk and Galbraith (1975) showed that highest coherences were observed between sites known to have anatomical connections.

In children below 3 years of age, coherences have an average value of 0.2—0.3 with occasional peaks as high as 0.6 (Shulte and Bell 1973; Joseph et al. 1975; Livanov 1977). In adults, coherences of 0.4—0.7 are commonly reported (Livanov 1977; Shaw et al. 1979; Weller and Montagu 1979). Montagu (1975) reported essentially adult values (0.5—0.7) for children with mean age of 5.6 years. No data were found on normative values for interhemispheric gain spectra.

This study was designed to explore the relationships of age and PbB to children's EEG, employing spectrum analysis techniques. Results on power spectra were to be compared with age effects reported in the literature and to be evaluated for PbB effects. Spectrum analysis methods were used to provide sensitive new indices of laterality.

Methods

Subjects and data collection

Subjects were selected from the same group as used in Otto et al. (1981), except that only data from the frequent-rare (FR) paradigm were used. Because different data windows were used and fewer trials were required, more subjects were available in this analysis. A total of 37 males and 32 females (65 Blacks and 4 Whites) was used. Means, standard deviations and ranges of age, IQ (Bayley or Stanford Binet), socioeconomic scale (Hollingshead Two-Factor Index of Social Position), number of trials per subject and PbB levels are shown in Table I.

TABLE I

Demographic characteristics of sample.

	Mean	S.D.	Minimum	Maximum
Age (months)	36.8	17.5	13	75
IQ	85.9	14.0	46	118
Socioeconomic scale	66.9	13.4	22	91
Trials	14.2	5.3	4	24
PbB	29.5	13.3	6	59

Analog-to-digital conversion and editing were the same as in Otto et al. (1981) except that data from left and right parietal (P3 and P4 in the 10-20 system) were used for spectrum analysis. Subjects were included if 4 or more artifact-free trials were avialable. One second pieces of data were used, beginning 0.5 sec after each rare stimulus.

Data reduction

Data were analyzed by a variety of spectrum analyses using Hanning weights. A fast Fourier transform was computed from each 1.0 sec piece of EEG data from both P3 and P4. Spectrum measures, described below, where then derived from these raw spectra which were averaged over all available trials for each subject. The dependent variables were therefore one of each kind of spectrum per subject. Logarithmic transformed power spectra were computed from the raw spectra (Bendat and Piersol 1971) in order to meet normal theory requirements for hypothesis testing.

Cross-spectra and laterality

Regression analysis was used to obtain one set of least squares estimates of laterality for each subject. The slope and intercept using P4 log powers as the dependent variable

and P3 log powers as the predictors were used as measures of relationship of P4 log power relative to P3. These terms are similar to averaged amplitude ratios and differences for each frequency band. Squared correlations between P3 and P4 log powers were used to describe the trialwise consistency of laterality for each subject.

Measures of relationship between bilaterally *synchronized* EEG (rather than total EEG) were also computed for each frequency band. The 3 spectra were the coherence, gain and phase between P3 and P4. These spectra were computed for each frequency band, from spectral quantities averaged across all trials (Benignus 1969).

Subjects in this study were awake with eyes open and since data were collected after a rare stimulus, very few high amplitude α waves developed. All of the measures of laterality as defined above, both for synchronized and total activity, are mathematically and physically meaningful even when no 'sinusoidal' wave activity is present.

Statistical analysis

Initially it was unclear how many frequency bands in the spectra should be used. To resolve this question all spectra were computed with the following 8 frequency bands: 1–2, 3–4, 5–6, 7–8, 9–10, 11–12, 13–16, and 17–20 Hz. A principal components analysis of a residual covariance matrix yielded an estimate of the structure of the dependent variables without the contaminating effects of the independent variables (Muller et al. 1979). After decisions about the principal components were made, statistical significance tests were made using the multiple regression technique described by Otto et al. (1981). Snooping procedures, such as principal component analysis, capitalize on chance relationships so that significance tests made during regression analysis are biased toward too many significant results. The high cost of a false negative and the cost and uniqueness of the data, made this approach necessary. Consequently, this study must be replicated before conclusions are firmly accepted. However, in view of the Bonferroni corrections applied to the repeated significance tests (see Table II), these results might still be viewed as more conservative than reported in other articles where uncorrected repeated tests are used.

A weighted least squares procedure was used to test a regression model with the spectrum measures as dependent variables. Observations were weighted by the square root of the number of trials for each subject in order to homogenize variances. Predictors were treated as 4 groups: (1) demographics (SES, IQ and sex), (2) age effects (linear, quadratic and cubic), (3) PbB effects (linear, quadratic and cubic), and (4) age by PbB interaction effects (age linear by PbB linear, age quadratic by PbB linear, PbB quadratic by age linear and age quadratic by PbB quadratic). Orthogonal polynomials for age and PbB were used to evaluate the linear, quadratic and cubic terms.

Each group of dependent variables was tested separately (e.g., gain for all bands). Each of the 4 groups of predictors was tested as a set in the order listed. If the first set was not significant, it was not included in the regression model, and the second set was tested. If a set was significant, stepdown tests were used to determine which variables in the set were to be included in the model. The ordering of sets was chosen so that demographic effects, if present, were controlled in tests of age and PbB, and effects of age were controlled in tests of PbB. Predicted trend lines and confidence intervals about the trend lines were produced for each model, as well as an estimate of the variance accounted for by the model.

Regression analysis was used to analyze these data because a continuous distribution of PbB values was observed. PbB values in this study ranged from 'normal' values to those slightly above normal (CDC 1978). Artificially dividing the sample into groups which could have been termed 'normal controls'

and 'moderate PbB' would have been a less sensitive procedure. Regression analysis permitted continuous comparisons across the entire range of PbB values.

Results

Principal components

Principal components analysis showed that only 4 frequency bands were required to describe spectra. These bands were 1–4 Hz (δ), 5–8 Hz (θ), 9–12 Hz (α), and 13–20 Hz (β). Also, log power spectra from P3 and P4 could be averaged together to produce a single, more stable spectrum, P3 + P4. Two of the spectral measures of laterality, phase and intercept, accounted for little variation among subjects (principal components) and were thus eliminated from hypothesis tests.

Significance tests

The 5 spectra included in the significance tests were (1) P3 + P4 log power spectrum, (2) slope spectrum, (3) squared correlation spectrum, (4) gain spectrum, and (5) coherence spectrum. Table II shows results of stepwise multivariate tests for these variables. Each test is multivariate because 4 frequency bands were tested. Overall tests for the 5 groups of dependent variables showed a simple pattern in which no demographic variables and no interactions were significant. P3 + P4 log power spectra, gain and coherence were significantly affected by age. Gain was affected by PbB. Each of the results which was significant was further explored.

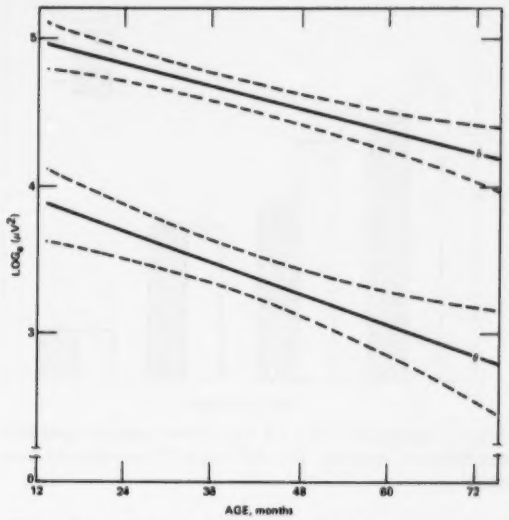


Fig. 1. P3 + P4 log power and 95% confidence bounds in the δ and θ frequency bands as a function of age. Estimated trend lines account for about 26% of variance in δ band, $P < 0.0001$, and about 22% in the θ band, $P < 0.0001$.

TABLE II

Results of multivariate tests from regression analysis. Numbers in the field of the table are P values. To keep family-wise type I error rate below $P < 0.1$ for each independent variable set, a P value in the table must be $P < 0.02$ in order to be declared significant (Kirk 1968).

	Demographic variables	Age	PbB	Pb by age interaction
P3 + P4 log power spectrum	0.31	0.0000003 *	0.26	0.15
Slope spectrum	0.69	0.12	0.052	0.12
Squared correlation spectrum	0.38	0.024	0.66	0.61
Gain spectrum	0.68	0.003 *	0.011 *	0.17
Coherence spectrum	0.12	0.0005 *	0.64	0.65

* Statistically significant.

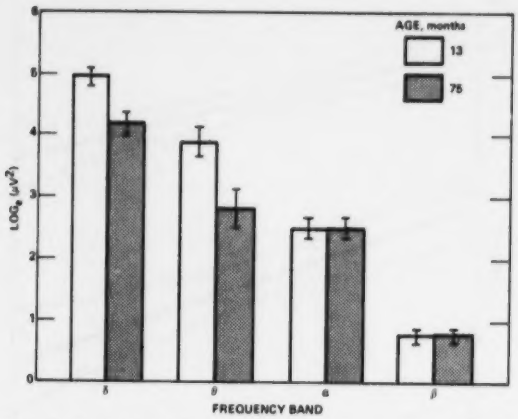


Fig. 2. Estimated P3 + P4 log power spectra and 95% confidence bounds for 13- and 75-month-old subjects.

Power spectra and age

Stepdown tests of the effect of age on log power spectra showed only an overall significant linear effect in only the δ and θ bands. Fig. 1 shows that δ and θ band log power declines as a function of age from 13 to 75 months. The 95% confidence bounds about the predicted lines are also shown. The estimated relationship accounts for about 26% of the variance in the δ band and about 22% in the θ band (multiple $r \approx 0.5$). Fig. 2 shows estimated log power spectra for ages 13 and 75 months, the youngest and oldest ages in this study.

Coherence spectra and age

Results of planned subtests on coherence spectra, which were significantly affected by age in the overall test, showed that only linear effects were significant, but that no single coherence band was by itself significantly related to age. Inspection of the canonical variates revealed that δ and α band coherences decreased, while θ and β band coherences increased as a function of age. Trend lines in this finding, however, had wide confidence limits. Since this pattern is not readily interpretable nor very strong,

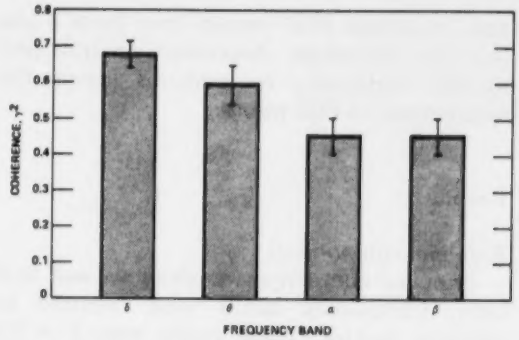


Fig. 3. Estimated grand mean coherence spectrum with 95% confidence bounds.

the grand mean coherence spectrum was computed (Fig. 3).

Gain spectra, age and PbB

Gain spectra were affected by both age and PbB. Stepdown tests revealed only linear effects and that only the δ band gain increased as a function of age (Fig. 4). Fig. 5 shows a plot of the grand mean gain spectrum for the 3 higher frequency bands and a

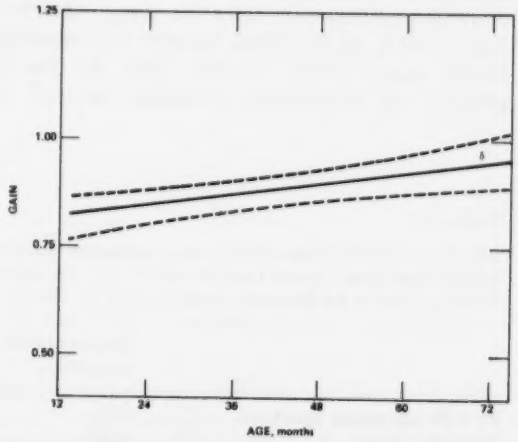


Fig. 4. Gain and 95% confidence bounds between P3 and P4 in the δ band as a function of age. Trend accounted for about 10% of the variance, $P < 0.01$. Values were estimated from the model for PbB values of 20 μg/dl.

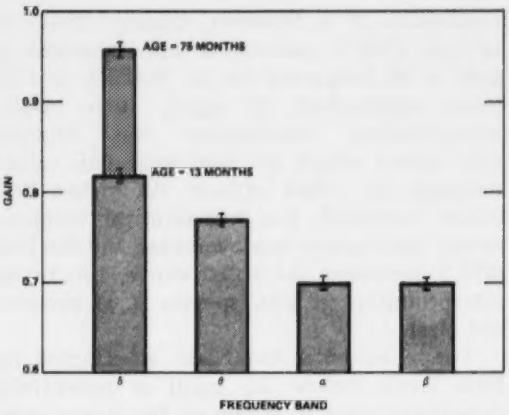


Fig. 5. Gain spectra with 95% confidence bounds for youngest and oldest ages in the study. Values were estimated from the model for PbB of 20 μg/dl. Only the δ-band coherence differed as a function of age.

double bar plot for the δ for 13- and 75-month-old subjects. These graphs were plotted for a PbB level of 20 μg/dl.

Evaluation of the effect of PbB on gain showed that only the cubic term was significant in all frequency bands. Fig. 6 shows a plot of the trend for gain in the δ band as a function of PbB, which is typical for all

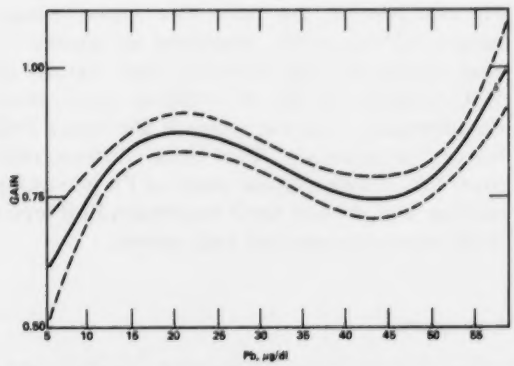


Fig. 6. Estimated cubic trend line and 95% confidence bounds for gain between P3 and P4 in the δ band as a function of Pb. Age was held at mean value of 36.8 months. Trend line accounted for about 20% of variance in δ band. Trends for θ, α and β bands were similar with variance accounted for of about 6%, 11% and 11%, respectively.

4 bands. The gain had a sharp increase below approximately 15 μg/dl, leveled off, decreased slightly between about 30 and 40 μg/dl and then rose sharply after 40 μg/dl.

Since gain was below unity for all frequency bands and subjects, it was implied that P3 was always greater in amplitude of synchronized EEG than P4. Since the estimate of gain spectra is biased, however, it was necessary to test the gain spectra for P4 predicting P3, and compare the results to P3 predicting P4. This was done for several combinations of age and PbB. In all cases for all frequency bands, the gain as estimated for P4 predicting P3 was higher than for P3 predicting P4. This tended to confirm the conclusion that P3 amplitude is higher than P4 amplitude when only synchronized EEG is considered.

Discussion

Log power spectra

Comparison of Fig. 1 with data in Matousek and Petersen (1973) reveals a remarkable agreement. An exception is that they reported an early increase in α-band power which was not observed in this study. Their data were collected from bipolar P3-O3 and P4-O4 electrodes while the data here were collected from monopolar P3 and P4 to linked ears. They used nearly 15 times as many subjects as this study so that a smaller effect could have been significant. Also, since subjects in this study were measured in the eyes open, stimulated condition, little rhythmic α occurred (see Fig. 2). It was therefore impossible to verify the reported gradual increase in α frequency as a function of age. Note that despite the fact that children were used as subjects, adult frequency values were used to define the α band. Since no rhythmic α waves were observed this produced no problems.

Laterality

The classical measures of laterality, slope

and squared correlation, were not significantly affected by age or PbB. The lack of age effects in these measures is in agreement with Giannitrapani et al. (1966), Joseph et al. (1976) and Varner et al. (1977).

It was shown that the δ-band gain increased linearly with age, but that the corresponding coherence did not vary with age in a similar or simple fashion. If it is assumed that coherence is constant over age, then perhaps signals are passed between hemispheres with more amplification as subjects mature. Another possibility is that some common signal source begins sending more signals to both hemispheres as age increases. Early δ activity, while of greater amplitude, is apparently more bilaterally random. As the subject matures the δ activity might be either brought under some common control or various sites might become more dependent upon each other. Whether this should be viewed as an increase in interhemispheric processing, a decrease in lateral specialization under these stimulation conditions, or some other change in function is not clear without further data.

It is noteworthy that for all subjects, regardless of age or PbB, the amplitude at P3 was estimated to be greater than at P4 for *synchronized* EEG. This represents an EEG laterality even in children well below 75 months in age. This tends to support the notion that the relative *synchronized* EEG amplitude is functionally important since behavioral handedness is reported to be present in children of this age range. Other measures of EEG laterality have not shown hemispheric differences in young children.

The magnitude of gain in all frequency bands was affected by PbB. While the effects followed a cubic trend and decreased as a function of PbB for mid-range values, the tendency was for gain to increase as a function of PbB of extreme values. In view of the number of subjects and the stepwise data analysis, it would not be wise to take the exact cubic trend too seriously without replication. It is, however, apparent that low or high PbB is associated with increases in gain in all frequency bands. Possibly as PbB levels approached 15 μg/dl, some bodily compensatory mechanism was brought into action which for mid-range PbB values managed to offset effects. As higher PbB values occurred, the hypothetical compensatory mechanism was overcome and the PbB effect increased. As noted above, functional interpretation of gain spectra is, at present, not clear.

The conclusion that gain is affected by PbB levels below 15 μg/dl is potentially important since it is one of the lowest-level PbB effects reported in the literature. If the functional interpretation of interhemispheric gain can be discovered, then PbB effects on behavior might be better understood. Since the effects are apparently present at 'normal' PbB levels, it is important that: (1) the functional nature of interhemispheric gain be explored, and (2) the PbB effect be replicated.

It is likely that PbB values observed in this study are lower than peak values which occurred in the past in these subjects. If that is so, then the relatively low PbB level effects shown in this study are in fact due to a higher Pb exposure in the past. The epidemiologic nature of this study precludes an answer to that question. The direction and nature of EEG effects of Pb in children have been documented, however, even if the exact PbB history is unknown. That none of these children had shown clinical signs of Pb poisoning implies that even at their maximum PbB levels their poisoning was not very severe.

Summary

This study explored the effects of age and PbB upon EEG power spectra and various measures of hemispheric laterality in children, aged 13—75 months, watching a display (cartoon). The following are the principle conclusions:

(1) The δ- and θ-band amplitude decreased with age.

(2) When only bilaterally *synchronized* EEG between P3 and P4 was considered, the amplitude of P3 was estimated as greater than P4 in all frequency bands and for all ages. Previous reports have not shown lateral EEG dominance in children below 75 months.

(3) When lateral dominance measures consider only the relationship between *synchronized* EEG at P3 and P4, bilateral communality in the δ band increased with age.

(4) Increased PbB generally produced an increase in the relative amplitude of *synchronized* EEG between P3 and P4 in all frequency bands. This was true for PbB levels well below 15 μg/dl, among the lowest level PbB effects previously reported. No clinical or behavioral effects of PbB values have been reported below 15 μg/dl.

It appears to be theoretically and practically important to understand the functional significance of bilaterally synchronized activity. The signal processing of the CNS can be explored using these methods. Greater understanding of these data would help define the extent and etiology of PbB effects on the CNS.

Résumé

Effets de l'âge et de la surcharge corporelle en plomb sur le fonctionnement du système nerveux central chez de jeunes enfants. II. Spectres EEG

Cette étude explore les effets de l'âge et de la surcharge en plomb (SPb) sur les spectres de puissance EEG et diverses mesures de latéralité hémisphérique chez l'enfant âgé 13—75 mois, en train de regarder une séquence visuelle (dessin animé). Les données suivantes sont les conclusions principales:

(1) L'amplitude de la bande delta et thêta diminue avec l'âge.

(2) Quand on considère seulement l'EEG *synchronisé* bilatéral entre P3 et P4, l'amplitude en P3 apparaît supérieure à celle en P4 dans toutes les bandes de fréquence et pour tous les âges. Les rapports antérieurs n'ont pas montré de dominance latérale EEG chez des enfants au-dessous de 75 mois.

(3) Quand les mesures de dominance latérale considèrent seulement la relation entre les EEG *synchronisés* en P3 et P4, la communauté bilatérale dans la bande delta augmente avec l'âge.

(4) La SPb produit généralement une augmentation de l'amplitude relative de l'EEG synchronisé entre P3 et P4 dans toutes les bandes de fréquence. Ceci est vrai pour des niveaux de SPb très inférieurs à 15 μg/dl, qui constituent les niveaux les plus bas jamais rapportés auparavant. Aucun effet clinique ni comportemental des valeurs du SPb n'ont été rapportés au-dessous de 15 μg/dl.

Il semble être important, d'un point de vue théorique et pratique, de comprendre la signification fonctionnelle de l'activité synchronisée bilatérale. Le traitement du signal du système nerveux central peut être exploré en utilisant ces méthodes. Une meilleure compréhension de ces données aiderait à définir l'étendue et l'étiologie des atteintes du système nerveux central par le SPb.

Supported by NIEHS Grant No. ES-01104, EPA Contract No. 68-02-1702, USPHS Grant No. HD-3110 and MCH Project 916. The authors wish to thank the many people who have assisted in this project, especially S. Schroeder, C. Milar, J. Dolcourt, L. Reiter and J. Nichols.

References

Bendat, J.S. and Piersol, A.G. Random Data: Analysis and Measurement Procedures. Wiley-Interscience, New York, 1971.

Benignus, V. Estimation of coherence spectrum and its confidence interval using the FFT. IEEE Trans. Audio-Electroacoust., 1969, AU-17: 145—150.

Bradley, J.E. and Powell, A.M. Oral calcium EDTA in lead intoxication of children. J. Pediat., 1954, 45: 297—301.

Burrows, N.F.E., Rendle-Short, J. and Hanna, D. Lead poisoning in children. Brit. med. J., 1951, 1: 329—334.

Busk, J. and Galbraith, G. EEG correlates of visual-motor practice in man. Electroenceph. clin. Neurophysiol., 1975, 38: 415—422.

Byers, R.K. and Maloof, C. Edathamil calcium-disodium (versenate) in treatment of lead poisoning in children. Amer. J. Dis. Child., 1954, 87: 559—569.

Donchin, E., Kutas, M. and McCarthy, G. Electrocortical indices of hemispheric utilization. In: S. Harnad, R.W. Doty, L. Goldstein, J. Jaynes and G. Krauthamer (Eds.), Lateralization in the Nervous System. Academic Press, New York, 1977: 339—384.

Fejerman, N., Gimenez, E., Vallejo, N. and Medina, C. Lennox's syndrome and lead intoxication. Pediatrics, 1973, 52: 227—234.

Galbraith, G. The effect of prior EEG 'coupling' upon the visual evoked response. IEEE Trans. bio-med. Engng, 1967, BME-14: 223—229.

Gersch, W. and Tharp, B.R. Spectral regression-amount of information analysis of seizures in humans. In: P. Kellaway and I. Petersen (Eds.), Quantitative Analytic Studies in Epilepsy. Raven Press, New York, 1976: 509—532.

Giannitrapani, D., Sorkin, A.I. and Enestein, J. Laterality preference of children and adults as related to interhemispheric EEG phase activity. J. neurol. Sci., 1966, 3: 139—150.

Hasselblad, V., Stead, A.G. and Galke, W. Analysis of coarsely grouped data from the lognormal distribution. J. Amer. statist. Ass., 1980, 75: 711—778.

Joseph, J.P., Lesèvre, N., Dreyfus-Brisac, C. and Reymond, A. Early development of interhemispheric synergy in the electroencephalogram of infants. In: M.A.B. Brazier (Ed.), Growth and Development of the Brain. Raven Press, New York, 1975: 255—273.

Joseph, J.P., Lesèvre, N. and Dreyfus-Brisac, C. Spatio-temporal organization of EEG in premature infants and full-term newborns. Electroenceph. clin. Neurophysiol., 1976, 40: 153—168.

Karpinski, F.E., Rieders, F. and Girsh, L.S. Calcium disodium versenate in the therapy of lead encephalopathy. J. Pediat., 1953, 42: 687—699.

Kirk, R.E. Experimental Design: Procedures for the Behavioral Sciences. Brooks/Cole, Belmont, Calif., 1968.

Livanov, M. Spatial Organization of Cerebral Processes. Halsted Press, New York, 1977.

Matousek, M. and Petersen, I. Automatic evaluation of EEG background activity by means of age-dependent EEG quotients. Electroenceph. clin. Neurophysiol., 1973, 35: 603—612.

Montagu, J. The hyperkinetic child: a behavioral, electrodermal and EEG investigation. Develop. Med. Child. Neurol., 1975, 17: 299—305.

Muller, K.E., Hosking, J.D. and Helms, R.W. Using Linmod to adjust for treatment effects when analyzing the covariance matrix. Proc. Amer. statist. Ass., 1979: 136—140.

Otto, D.A., Benignus, V.A., Muller, K.E. and Barton, C. Effects of age and body lead burden on CNS function in young children. I. Slow cortical potentials. Electroenceph. clin. Neurophysiol., 1981, 52: 229—239.

Schulte, F. and Bell, E. Bioelectric brain development. Neuropädiatrie, 1973, 4: 30—45.

Shaw, J., Brooks, S., Colter, N. and O'Connor, K. A comparison of schizophrenic and neurotic patients using EEG power and coherence spectra. In: J. Gruzelier and P. Flor-Henry (Eds.), Hemisphere Asymmetries of Function in Psychopathology. Elsevier/North-Holland, Amsterdam, 1979: 257—284.

Smith, H., Baehner, R., Curney, T. and Majors, W. The sequelae of pica with and without lead poisoning. Amer. J. Dis. Child., 1963, 105: 609—616.

Thurston, D., Middelkamp, J. and Mason, E. The late effects of lead poisoning. J. Pediat., 1955, 47: 413—423.

Varner, J.L., Ellingson, R.J., Danahy, T. and Nelson, B. Interhemispheric amplitude in the EEGs of full-term newborns. Electroenceph. clin. Neurophysiol., 1977, 43: 846—852.

Weller, M. and Montagu, J. Electroencephalographic coherence in schizophrenia: a preliminary study. In: J. Gruzelier and P. Flor-Henry (Eds.), Hemisphere Asymmetries of Function in Psychopathology. Elsevier/North-Holland, Amsterdam, 1979: 285—292.